UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,040	06/23/2004	Hans-Michael Eggenweiler	MERCK-2893	5203

23599 7590 05/02/2007

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
MOORE, SUSANNA	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
05/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,040	EGGENWEILER ET AL.	
	Examiner	Art Unit	
	Susanna Moore	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,13,14,22-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9,13,14 and 22-30* is/are allowed.

6)☒ Claim(s) *31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/2/2007 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. Regarding claim 31, the phrase "a disease or disorder caused by the PDE VII isozyme in its role in regulating the activation and degranulation of human eosinophils" renders the claim indefinite because it is unclear what Applicant regards as the invention. It is unclear as to what diseases are caused by PDE VII in this role versus diseases that are caused by PDE VII in some other role. There is incomplete knowledge of PDE VII in human diseases. Furthermore, what diseases cause or are caused by the inhibition of PDE VII? There is no standard list.

Claim 31-32 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims.

(a) Scope of the compounds. The instant claim embraces nine compounds with a substituted pyrrolopyrimidine scaffold with several substituents at three positions.

(b) Scope of the enzymes covered. Claim 31 is drawn to "a disease or disorder caused by the PDE VII isozyme in its role in regulating the activation and degranulation of human eosinophils" which renders the scope unknown. Claim 32 is drawn to a method of treating an inflammatory diseases, autoimmune diseases, a memory disorder, skin diseases, transplant rejection, tumour growth or tumor metastasis, AIDS, an allergic disease, and the others listed. The scope for several of the ones mentioned above will be discussed in more detail.

An inflammatory disease can be defined as a disease characterized by inflammation anywhere in the body. Inflammation is the body's first response to injury, e.g. trauma, infection irritation, etc. This is a non-specific immune response. Inflammation has two main components - cellular and exudative.

The exudative component involves the movement of fluid, usually containing many important proteins such as fibrin and immunoglobulins (antibodies). Fibrinogen is important for clot formation and the prevention of further loss of blood. Immunoglobulins may act as specific or nonspecific *opsonins* facilitating thus the process of phagocytosis, or may participate in antibody-dependent cell-mediated cytotoxicity (ADCC) by which target cells are destroyed by killer cells. Blood vessels are dilated upstream of an infection (causing redness and heat) and constricted downstream while capillary permeability to the affected tissue is increased, resulting in a net loss of blood plasma into the tissue - giving rise to edema or swelling. The swelling distends the tissues, compresses nerve endings, and thus causes pain.

The cellular component involves the movement of white blood cells from blood vessels into the inflamed tissue. Professional phagocytes (neutrophils, eosinophils, monocytes and tissue macrophages) are essential performing phagocytosis, lymphocytes are involved in the specific immune responses, endothelial cell in the regulation of leukocyte emigration from the blood into inflamed tissue and platelets with mast cells in the production of early phase mediators.

For the possibility of surrounding tissue damage, inflammatory responses must be well ordered and controlled. The body must be able to act quickly in some situations, for example to reduce or stop the lost of blood, whereas tissue repair and reconstruction can begin a little later. Therefore, a wide variety of interconnected cellular and humoral (soluble) mechanisms are activated when tissue damage and infection occur. The body has the capacity to respond to both minor injuries such as bruising, scratching, cuts, and abrasions, as well as to major injuries such as severe burns and amputation of limbs.

Some examples of inflammatory diseases are as followed, but not limited to: allergies, appendicitis, arteritis, arthritis, asthma, blepharitis, bronchiolitis, bronchitis, bursitis, cervicitis, cholangitis, cholecystitis, chorioamnionitis, colitis, conjunctivitis, cystitis, dacryoadenitis, dermatitis, dermatomyositis, encephalitis, endocarditis, endometritis, enteritis, enterocolitis, epicondylitis, epididymitis, fasciitis, fibrositis, gastritis, gastroenteritis, gingivitis, hepatitis, hidradentitis supparativa, ileitis, immune reconstitution inflammatory syndrome (IRIS), laryngitis, mastitis, meningitis, myelitis, myocarditis, myositis, nephritis, omphalitis, oophoritis, orchitis, osteitis, otitis, pancreatitis, parotitis, pelvic inflammatory disease (PID), pericarditis, peritonitis, pharynx, pleuritis, phlebitis, pneumonitis, protitis, prostatitis, rhinitis, salpingitis, sinusitis, stomatitis, synovitis, tendonitis, tonsillitis, uveitis, vaginitis, vasculitis and vulvitis.

The immune system is the body's defense against infectious organisms and other invaders. Through a series of steps called the immune response, the immune system attacks antigens, which are not recognized by the body, and are destroyed by the immune system.

The immune system is made up of a network of cells, tissues, and organs that work together to protect the body. The key organs of the immune system are thymus, spleen, bone marrow, lymph vessels, lymph nodes and secondary lymphatic tissues such as tonsils, adenoids, and skin.

The immune system is often divided into two sections. One being innate immunity which is comprised of hereditary (always there) components that provide an immediate "first-line" of defense to continuously ward off pathogens.

The second is adaptive immunity, which is triggered when an antigen is detected. Several types of cells work together to recognize and respond to it. These cells trigger the B lymphocytes to produce antibodies. Antibodies are specialized proteins that lock onto specific antigens. Antibodies and antigens fit together like a key and a lock. Although antibodies can recognize an antigen and lock onto it, they are not capable of destroying it without help. That is the job of the T cells. The T cells are part of the system that destroys antigens that have been tagged by antibodies or cells that have been infected or somehow changed.

Sometimes a person is born with an overzealous immune system. When this occurs the immune system is intack and present but not working properly. In these cases, the immune system fails to properly distinguish between self and non-self, and attacks a part of the the body. Diseases which are associated with this type of disorder of the immune system are called

autoimmune disorders.

Some examples of autoimmune disorders are as follows, but not limited to: acute disseminated encephalomyelitis (ADEM), Addison's disease, antiphospholipid, aplastic anemia, autoimmune hepatitis, Coeliac disease, Crohn's disease, type I diabetes mellitus, Goodpasture's syndrome, Graves' disease, Guillain-Barré syndrome (GBS), Hashimoto's disease, lupus erythematosus, multiple sclerosis, myasthenia gravis, opsoclonus myoclonus syndrome (OMS), optic neuritis, Ord's thyroiditis, pemphigus, primary biliary cirrhosis, psoriasis, rheumatoid arthritis, Reiter's syndrome, Takayasu's arteritis, temporal arteritis, warm autoimmune hemolytic anemia and Wegener's granulomatosis.

Memory is the process by which people encode, store and retrieve information. Encode refers to the initial perception and registration of information. Storage is the retention of encoded information over time. Retrieval refers to the processes involved in using stored information. Whenever people successfully recall a prior experience, they must have encoded, stored, and retrieved information about the experience. Conversely, memory failure, for example, forgetting an important fact, reflects a breakdown in one of these stages of memory.

Memory and learning are closely related, and the terms often describe roughly the same processes. The term learning is often used to refer to processes involved in the initial acquisition or encoding of information, whereas the term memory more often refers to later storage and retrieval of information. However, this distinction is not hard and fast. After all, information is learned only when it can be retrieved later, and retrieval cannot occur unless information was

learned. Thus, psychologists often refer to the learning/memory process as a means of incorporating all facets of encoding, storage, and retrieval.

The term long-term memory is somewhat of a catch-all phrase because it can refer to facts learned a few minutes ago, personal memories many decades old, or skills learned with practice. Generally, however, long-term memory describes a system in the brain that can store vast amounts of information on a relatively enduring basis.

There are many environmental factors and diseases which affect long term memory and learning functions, including, but not limited to: anterograde amnesia, retrograde amnesia, dissociative amnesia, infantile amnesia, multiple personality disorders, Alzheimers disease, psychoactive drugs, dietary deficiencies, electroconvulsive therapy, head injuries, alcoholism, aging, lacunar amnesia, fugue state, global amnesia, posthypnotic amnesia, source amnesia, memory distrust syndrome, attention deficeit disorder (ADD), vascular dementia (including Binswanger's disease), dementia with Lewy bodies, frontotemperol lobal degeneration (including Pick's disease), Huntington's disease, Parkinson's disease, HIV infection, semantic dementia, progressive nonfluent aphasia, Creutzfeldt-Jakob disease and depression.

Skin diseases are any diseases that affect the skin. The following includes a list of such diseases, but is not limiting to: acne, actinic keratosis, angioma, athlete's foot, aquagenic pruritus, atopic dermatitis, baldness, basal cell carcinoma, bed sore, Behcet's disease, blepharitis, boil, Bowen's disease, bullous pemphigoid, canker sore, carbuncles, cellulitis, chloracne, chronic dermatitis, cold sores, contact dermatitis, creeping eruption, dandruff, dermatitis, dermatitis herpetiformis, dermatofibroma, diaper rash, dyshidrosis, eczema, epidermolysis bullosa,

erysipelas, erythroderma, Ferguson's Disease, friction blister, hidradenitis suppurativa, hyperhidrosis, ichthyosis, impetigo, jock itch, kaposi's sarcoma, keloid, keratoacanthoma, keratosis pilaris, lice infection, lichen planus, lichen simplex chronicus, lipoma, lymphadenitis, malignant melanoma, melasma, miliaria, molluscum contagiosum, nummular dermatitis, Paget's disease of the nipple, pediculosis, pemphigus, perioral dermatitis, photoallergy, photosensitivity, pityriasis rosea, pityriasis rubra pilaris, porphyria, psoriasis, Raynaud's disease, ring worm, rosacea, scabies, scleroderma, sebaceous cyst, seborrheic keratosis, seborrhoeic dermatitis, shingles, skin cancer, skin tags, spider veins, squamous cell carcinoma, stasis dermatitis, tick bite, tinea barbae, tinea capitis, tinea, corporis, tinea cruris, tinea pedis, tinea unguium, tinea versicolor, tinea, tungiasis, urticaria, vitiligo and warts.

Cancers are classified by the type of cell that resembles the tumor and, therefore, the tissue presumed to be the origin of the tumor. The following general categories are usually accepted:

- Carcinoma: malignant tumors derived from epithelial cells.
- Lymphoma and Leukemia: malignant tumors derived from blood and bone marrow cells
- Sarcoma: malignant tumors derived from connective tissue, or mesenchymal cells.
- Mesothelioma: tumors derived from the mesothelial cells lining the peritoneum and the pleura.
- Glioma: tumors derived from glia, the most common type of brain cell.
- germ cell tumours: tumors derived from germ cells, normally found in the testicle and ovary.
- Choriocarcinoma: malignant tumors derived from the placenta.

Cancers include the following, but are not limited to: (topography) eye, endometrium,

bladder, breast, colon, penis, kidney, liver, lung, brain, small cell lung cancer, esophogus, gall bladder, ovary, pancreas, stomach, cervix, colon/rectum, mouth, larynx, head/neck, thyroid, prostate, testicle, skin, squamous cell carcinoma, anus and leukemia; (cell type/morphology) acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma, Burgett's lymphoma, acute myelogenous leukemia, chronic myelogenous leukemia, myelodyplastic syndrome, promyelocytic leukemia, fibrosarcoma, rhabdomyosarcoma, astrocytoma, neuroblastoma, glioma, schwannomas, melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer, Kaposi's sarcoma, angiosarcoma, dermatofibrosarcoma, desmoid tumor, desmoplastic small round cell tumor, extraskeletal chondrosarcoma, extraskeletal osteosarcoma, hemangiopericytoma, hemangiosarcoma, leiomyosarcoma, liposarcoma, lymphangiosarcoma, malignant fibrous histiocytoma, neurofibrosarcoma, synovial sarcoma, Askin's Tumor, Ewing's sarcoma and alignant hemangioendothelioma.

Note, tumors include neoplastic and non-malignant tumors.

(B) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) Direction or Guidance: The dosage range information, found on page 76 of the Specification gives 5-50 mg/kg. Moreover, this is generic, the same for the many disorders covered by the Specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for any and all diseases associated with all the diseases covered by the Scope of diseases listed above.

(D) State of the Prior Art: These compounds are substituted pyrrolopyrimidine compounds. So far as the examiner is aware, no substituted pyrrolopyrimidine compounds of any kind have been used for the treatment of any or all the diseases covered by the Scope of diseases above.

The state of the clinical arts in therapeutic diseases is such that as of 2005, there were no therapeutic uses for inhibiting PDE7. An articled titled, "PDE7 Inhibitors," (Expert. Opin. Ther. Patents, 2002, 12(4), 601-603) recites "...PDE7 inhibitors may be useful in the treatment of asthma and allergic diseases...". While the article mentions a therapeutic potential of PDE7 inhibitors for the treatment of asthma and allergic diseases, it is only suggestive of a utility for PDE7 inhibitors. Thus, the use is just a possibility. In fact, Beavo et. al. (Science, 1999, 283, 848-850), only "suggests that PDE7 may be a good target for selective therapeutic modulation of T cell responsiveness." Here again, the article only raises this one possibility. Lastly, Castro et. al. (Med. Res. Rev., 2005, 25(2), 229-244) states "PDE7 has the potential to regulate human T cell functions...However, its specific role in T cell function is still unclear...". Their potential remains at the level of speculation. As of the filing date, there are no references, which provide firm evidence that inhibition per se of PDE7 isoforms is of any established use.

The prior art knows that there never has been a compound capable of treating cancer generally. "The cancer therapy art remains highly unpredictable, and no example exists for efficacy of a single product against tumors generally." (<http://www.uspto.gov/web/offices/pac/dapp/1pecba.htm#7 <http://www.uspto.gov/web/offices/pac/dapp/1pecba.htm>> ENABLEMENT DECISION TREE, Example F, situation 1) There are compounds that treat a modest range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology.

Rheumatoid arthritis itself can be treated only with compounds or drugs that suppress alpha tumor necrosis factor (TNF), e.g. Enbrel, Humira and Remicade. Applicants compounds are not disclosed to block alpha TNF, let alone is their evidence that they do. The skill of one in the art is such that only such agents have been made to work.

AIDS can only be treated with anti-virals, a property these compounds not disclosed to have.

There are two forms of diabetes, type I and type II. Type I, formerly known childhood diabetes, is characterized by loss of the insulin-producing beta cells of the islets of Langerhans of the pancreas leading to a deficiency of insulin. Currently, type 1 diabetes can be treated only with insulin. Type II, previously known as adult-onset diabetes, is due to a combination of defective insulin secretion and defective responsiveness to insulin (often termed insulin resistance or reduced insulin sensitivity), almost certainly involving the insulin receptor in cell

membranes. Type II diabetes is treated with sulfonylureas, meglitinides, biguanides, thiazolidinediones, alpha glucosidase inhibitors, incretin mimetic and insulin as a last resort.

(E) Working Examples: The Applicant has not provided any working examples to any utility. Applicant, on page 3 of the Specification presents a prophetic biological assay for the establishment of the IC50 of a PDE VII inhibitor. Moreover, of the different isoforms currently known for PDE7, i.e. PDEA1, PDEA2, PDEA3 and PDEB, the inhibition assays do not discriminate as to which isoform, if any one, was used for the assay.

(F) Skill of those in the art: Even after the filing date of this case, research shows only the possibility of treating inflammation with a PDE7 inhibitor. Castro et. al. (Med. Res. Rev., 2005, 25(2), 229-244) states "PDE7 has the potential to regulate human T cell functions...However, its specific role in T cell function is still unclear...". As of 2005, there are no references, which provide conclusive evidence that the method of use or method of treatment is enabled for PDE7 inhibitors.

(G) The quantity of experimentation needed: Owing especially to factors A, C, E and F, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the

claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims.

(a) Scope of the compounds. The instant claim embraces nine compounds with a substituted pyrrolopyrimidine scaffold with several substituents at three positions.

(b) Scope of the enzymes covered. Claim 32 is drawn to a method of treating heart disease, reversible or irreversible myocardial ischaemia/reperfusion damage, acute or chronic heart failure or restenosis. The scope for several are outlined below.

Stenosis is the narrowing of a blood vessel or other tubular organ. Restenosis just means the recurrence of this condition. There are different causes, such as atherosclerosis, birth defects, ischaemia, infection, neoplasm and inflammation. Examples of various stenotic lestions are, but not limited to: intermittent claudication (peripheral artery stenosis), angina (coronary artery stenosis), obstructive jaundice (biliary tract stenosis), carotid artery stenosis (strokes and transient ischaemic episodes), pyloric stenosis (gastric outflow obstruction), renal artery stenosis, hydrocephalus, stenosing tenosynovitis, spinal stenosis, subglottic stenosis (SGS) and bowel obstruction.

Heart disease is one of a number of different diseases which afflict the heart. The most common heart diseases are (www.wikipedia.com):

- heart disease, the end result of the accumulation of atheromatous plaques within the walls of the arteries that supply the myocardium
- Ischaemic heart disease, a disease characterized by reduced blood supply to the heart.
- Cardiovascular disease, a class of diseases that involve the heart and/or blood vessels (arteries and veins).Implies under this category some popular diseases like: diabetes, high blood pressure and hypercholesterolemia.
- Pulmonary heart disease, a failure of the right side of the heart.

- Hereditary heart disease
- Hypertensive heart disease
- Inflammatory heart
- valvular heart disease

(B) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) Direction or Guidance: The dosage range information, found on page 76 of the Specification gives 5-50 mg/kg. Moreover, this is generic, the same for the many disorders covered by the Specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for any and all diseases associated with all the diseases covered by the Scope of diseases listed above.

(D) State of the Prior Art: These compounds are substituted pyrrolopyrimidine compounds. So far as the examiner is aware, no substituted pyrrolopyrimidine compounds of any kind have been used for the treatment of any or all the diseases covered by the Scope of diseases above.

(E) Working Examples: The Applicant has not provided any working examples to any utility. Applicant, on page 3 of the Specification presents a prophetic biological assay for the establishment of the IC50 of a PDE VII inhibitor. Moreover, of the different isoforms currently known for PDE7, i.e. PDEA1, PDEA2, PDEA3 and PDEB, the inhibition assays do not discriminate as to which isoform, if any one, was used for the assay.

(F) Skill of those in the art: Even after the filing date of this case, research shows only the possibility of treating inflammation with a PDE7 inhibitor. Castro et. al. (Med. Res. Rev., 2005, 25(2), 229-244) states "PDE7 has the potential to regulate human T cell functions...However, its specific role in T cell function is still unclear...". As of 2005, there are no references, which provide conclusive evidence that the method of use or method of treatment is enabled for PDE7 inhibitors.

(G) The quantity of experimentation needed: Owing especially to factors A, C, E and F, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susanna Moore whose telephone number is (571) 272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SM

Mark L. Berch
Primary examiner
Art Unit 1624
Technology Center 1600